



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2006-D-0036] (formerly Docket No. 2006D-0344)

Draft Guidance for Industry on Drug Interaction Studies--Study Design, Data Analysis, Implications for Dosing, and Labeling Recommendations; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a revised draft guidance for industry entitled “Drug Interaction Studies--Study Design, Data Analysis, Implications for Dosing, and Labeling Recommendations.” The revised draft guidance is intended to provide recommendations for sponsors of new drug applications (NDAs) and biologics license applications (BLAs) for therapeutic biologics regarding in vitro and in vivo studies of drug metabolism, drug transport, and drug-drug, or drug-therapeutic protein interactions.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this revised draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the revised draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-

0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

Submit electronic comments on the draft guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a revised draft guidance for industry entitled “Drug Interaction Studies -- Study Design, Data Analysis, Implications for Dosing, and Labeling Recommendations.” Drug interactions can result when one drug alters the pharmacokinetics of another drug or its metabolites. Drug interactions also can reflect the additive nature of the pharmacodynamic effect of either drug when taken with the other drug. The main focus of this draft guidance is pharmacokinetic drug interactions. The revised draft guidance reflects the Agency’s view that the pharmacokinetic interactions between an investigational new drug and other drugs should be defined during drug development, as part of an adequate assessment of safety and effectiveness. It is important to understand the nature and magnitude of drug-drug interactions for several reasons. Concomitant medications, dietary supplements, and some foods, such as grapefruit juice, may alter metabolism and/or drug transport abruptly in individuals who previously had been receiving and tolerating a particular dose of a drug. Such an abrupt alteration in metabolism or transport can change the known safety and efficacy of a drug.

The revised draft guidance provides recommendations for sponsors of NDAs and BLAs regarding in vitro and in vivo studies of drug metabolism, drug transport, and drug-drug, or drug-therapeutic protein interactions. Namely, the guidance describes in vitro study methodologies, criteria for in vivo studies, in vivo study design, and data analysis in the context of identifying potential drug interactions. The guidance also addresses the implications of drug interactions for dosing and labeling.

In the Federal Register of September 12, 2006 (71 FR 53696), FDA announced the availability of a draft guidance entitled “Drug Interaction Studies--Study Design, Data Analysis, and Implications for Dosing and Labeling.” Comments were received and have been considered

during revision of the draft guidance. In addition, new developments in the field have been incorporated to reflect the Agency's current thinking. The Agency is publishing the draft guidance as a revised draft guidance to collect additional public comments. The revised draft guidance includes detailed discussion of several major changes, including the following: (1) When transporter-mediated drug interaction information is needed (including decision-trees); (2) drug-therapeutic protein interactions, (3) the utility of pharmacogenetic data; and (4) the use of physiologically based pharmacokinetic modeling.

This revised draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on conducting drug interaction studies during drug development to support marketing approval. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirement of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This revised draft guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR 201.57 have been approved under OMB control number 0910-0572.

III. Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) either electronic or written comments regarding this document. It is only necessary to send one set of comments. Identify comments with the docket number found in

brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances> or <http://www.regulations.gov>.

Dated: February 15, 2012.

Leslie Kux,

Acting Assistant Commissioner for Policy.

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